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# **How psychopathological factors affect both the onset of and recovery from Transient Global Amnesia**

**Short title: Role of psychopathological factors in TGA**

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To the Editor:

In a previous study (Quinette et al., 2006) we highlighted 4 subgroups of transient global amnesia (TGA) linked with different risk factors, one of which was the presence of personality disorders. We went deeper into this classification by collecting additional measures of psychopathological factors (anxiety and depression), in 38 patients (28 included in our preceding study and 10 new patients). Four subgroups of patients were also distinguished, one of whom was characterized by both emotional precipitants and previous or current anxious / depressive disorders (Figure 1). This latent psychological fragility associated with an intense emotional experience could help to trigger a TGA (Inzitari et al., 1997). The aim of the present research was to study the influence of these psychopathological factors on early recovery process (namely the day after the episode). Thus, we investigated the mood congruency effect in order to gain a better understanding of the influence of anxiety/depression on both the acquisition and retrieval of emotional episodic memories.

## METHOD

We reported data collected in 9 of 10 new patients included in the cluster analysis (Figure 1) and we divided this group of patients into two subgroups (“emotional” and “non-emotional”), according to their level of anxiety/depression as measured with the same scales and cut-off points as in the cluster analysis. The “emotional” (mean score of anxiety / depression: 63 / 10.5) and “non-emotional” groups (mean score of anxiety / depression: 50.6 / 2.6) included four and five patients, respectively. These groups were similar in age and duration of TGA episode. Control group included 13 healthy subjects (mean score of anxiety and depression: 46.9 and 2.5). All patients gave their informed consent to the study, which was performed in compliance with the Declaration of Helsinki.

[Insert Figure 1]

### **Anterograde component of episodic memory**

During the study session, the participants had to learn (intentional encoding) a list of 45 words (15 positive, 15 negative and 15 neutral items). Retrieval was assessed by means of a dual forced recognition task. An accuracy score corresponding to  $A'$  (Gardiner et al., 2002) was obtained for each word valence.

### **Retrograde component of episodic memory**

An autobiographical memory task, derived from Piolino *et al.*'s semi-structured questionnaire (2003), allowed us to gauge the ability to recall specific events across three time periods and to control both the intensity and valence of memories.

Inter-group comparisons were made by means of Mann Whitney Test. However, since only two patients in the “emotional group” carried out the autobiographical memory task, their performances were compared with normal controls according to the z score method.

## **RESULTS**

### **Anterograde component of episodic memory**

A group effect ( $p=0.04$ ) was found for the accuracy score of negative words between controls ( $A' = 0.88$ ) and the “emotional group” ( $A' = 0.76$ ). These patients had greater difficulty than controls distinguishing negative hits from lures. There was no statistical difference between controls and the “non-emotional” group ( $A' = 0.85$ ). No significant difference was found for positive ( $A' = 0.85$  for “emotional group,  $A' = 0.84$  for “non-emotional” group and  $A' = 0.86$  for control group) and neutral words ( $A' = 0.87$  for “non-emotional” group, and  $A' = 0.86$  for “emotional group” and control group).

### **Retrograde component of episodic memory (Table 1)**

The two patients of “emotional group” scored like controls for the two most recent periods, but their most remote memories were less specific and less intense than those of

controls. Moreover, valence scores for this period bordered on the significance threshold for z scores, meaning that they tended to provide more negative memories than controls. No statistical difference was found between the scores of the “non-emotional” group and the control group. In order to compare these groups more effectively, we also calculated z scores for the “non-emotional” group. No z scores were pathological (data not shown).

[Insert Table 1]

## DISCUSSION

Some studies (Guillery-Girard et al., 2005) highlighted several profiles of recovery after a TGA. Our study confirms this result and shows that only TGA patients with an anxious and/or depressive profile had persistent cognitive deficits in episodic memory. On the task assessing the anterograde component of episodic memory, these patients had difficulty distinguishing targets from lures, and only did so in the case of negative items. This “semantic cohesiveness” phenomenon, already observed in depression (Danion et al., 1995), is explained by the semantic closeness of emotional words which then act as “related lures” and lead to a high proportion of false alarms. This effect limited to negative words reflects a phenomenon of mood congruency (Tarsia et al., 2003). Patients with an anxious or depressive vulnerability produced less specific, less intense and even more negative memories for the most distant period, which corresponds to the “reminiscence bump”, usually characterized by detailed and happy memories (Berntsen & Rubin, 2002; Piolino et al., 2006). Furthermore, it has been shown (D'Argembeau et al., 2003) that negative memories are less episodic than positive ones. Thus, our results suggest that anxiety and depression might slow the recovery process and even prevent a full recovery.

While not questioning the organic nature of TGA, the emotional state of patients and the events surrounding the episode suggest that in some patients, psychogenic factors may intervene (Lucchelli & Spinnler, 2002). Kopelman (2000) has proposed a revised model of

amnesia, in which all types of amnesia take place along the same continuum according to the contribution of organic and psychogenic factors to their aetiology. Given this hypothesis, the two subgroups of TGA patients (with or without psychopathological disorders) would be situated at different points of the continuum. Whereas some TGA would be closely linked to the concept of psychogenic amnesia i.e. triggered by psychopathological factors, other kinds of TGA would be entirely due to organic factors.

In conclusion, our study shows that psychopathological factors are a central issue in the onset of and recovery from TGA. However, further studies combining psychopathological, neuropsychological and neuroimaging approaches need to be performed to confirm the influence of psychopathological factors in TGA.

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**Fig. 1:**

A hierarchical cluster analysis was carried out with same clinical variables than those used in the study of Quinette et al. (2006). 2 new measures were added: level of anxiety (with a cut off point of 55 in Spielberger Trait Anxiety Inventory, 1983) and depression (with a cut off point of 8, in Beck Depression Inventory , 1974). The results shows four clusters: 1/ TGA preceded by physical precipitants 2/ TGA preceded by emotional episodes accompanied by psychopathological factors 3/ patients with vascular risk factors 4/ TGA with no particular characteristics. The cluster in boldface includes all the emotional characteristics.

Table 1: Performances by TGA patients and normal controls on the autobiographical task.

<i>Lifetime period</i>	<b>Non-emotional group (n = 5)</b>		<b>Emotional group (n = 2)</b>		<b>Control group (n = 13)</b>	
	m	S.D.	<b>P04</b>	<b>P08 [z score]</b>	m	S.D.
<b><i>18-30 years</i></b>						
Specificity score	3.6	(0.42)	2.0 [-3.86] *	2.0 [-3.86] *	3.6	(0.4)
Intensity of memories	4.7	(0.99)	2.2 [-2.06] *	1,5 [-2.78] *	4.4	(1.0)
Emotional valence of memories	5.0	(0.97)	1.7 [-1.75]	2.0 [-1.58]	4.2	(1.4)
<b><i>Last 5 years (except last 12 months)</i></b>						
Specificity score	3.2	(0.76)	3.5 [0,15]	2,5 [-0.83]	3.3	(1.0)
Intensity of memories	4.3	(0.82)	4.2 [+0.28]	4,7 [+0,68]	3.9	(1.2)
Emotional valence of memory	4.2	(1.41)	5.7 [+2.11]	3.0 [-0.19]	3.2	(1.1)
<b><i>Last 12 months</i></b>						
Specificity score	3.4	(0.82)	2.0 [-1.41]	3.0 [-0.33]	3.3	(0.9)
Intensity of memories	3.5	(1.06)	2.0 [-1.02]	5.5 [+1.53]	3.4	(1.3)
Emotional valence of memory	4.7	(1.09)	2.0 [-1.39]	2.7 [-0.81]	3.8	(1.3)

m = average ; S.D.=standard deviation; P04/P08 corresponds to code of each patient

The pathological z score (calculated according to the number of controls and a threshold of .05) was 1.78.

Two specific memories (specificity score, Piolino et al., 2003) were requested for each lifetime period (18-30 years old, last 5 years except the last 12 months, and last 12 months). After each production, patients were asked to rate valence and intensity of memory. The mean scores of control and non-emotional group are presented. The scores of TGA patients belonging to the emotional group are reported individually.